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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

In re application of:	)	Examiner: Chunduru, Suryaprabha
Madou, et al.	)	
Serial No.: 09/905,041	)	Art Unit: 1637
Filed: July 13, 2001	)	
For: MULTIMERIC BIOPOLYMERS AS	)	Attorney Docket No.: 22727/04096
STRUCTURAL ELEMENTS AND	)	
SENSORS AND ACTUATORS IN	)	
MICROSYSTEMS	)	

Assistant Commissioner for Patents  
Washington, D.C. 20231

DECLARATION UNDER 37 CFR § 1.132

Dear Sir:

I, Dr. Leonidas G. Bachas, an inventor of the above-identified application state as follows:

1. I received a Bachelor of Science in Chemistry in 1981 from the University of Athens (Greece) and a Doctor of Philosophy Degree in Chemistry from the University of Michigan (Ann Arbor) in 1986. I was a postdoctoral associate at the University of Michigan between January and July 1986. I am the Frank J. Derbyshire Professor of Analytical and Biological Chemistry at the University of Kentucky, the Director of the Integrated Sensing Architectures program at the University of Kentucky and the

Associate Director of the University of Kentucky Superfund Program. I am also the author or co-author of 139 publications relating to Analytical and Biological Chemistry.

2. Amended Claims 1, 12, and 41 of the above-described application, which are shown in the attached Appendix, are all drawn to a multimeric biopolymer that is composed of a plurality of monomeric units including proteins, polypeptides, nucleic acids, and aptamers. Claims 1, 12, and 41 as amended also recite that the monomeric units of the present biopolymer are covalently linked. Claims 1, 12, and 41, as amended, also recite that a plurality of the monomeric units comprise a binding region or site for binding to a ligand or analyte selected from the group consisting of a sugar, a peptide, a nucleic acid, a hormone, a vitamin, a co-factor, an anion and a cation.
3. I have reviewed U.S. Patent No. 4,478,914 which issued to Geise on October 23, 1984. (hereinafter referred to as "Giese"). The multilayer structure that is described in Giese consists of alternating layers of molecules of the vitamin biotin (or a biotin-extender) and the protein avidin (See Figure 1 of Giese). Unlike the monomeric units of amended claims 1, 12, and 41 of the present application, the monomeric units of the Giese structure, i.e., biotin (or biotin-extender) and avidin are not covalently linked. Since biotin is a ligand for avidin, the biotin (or biotin-extender) molecules of the Giese multilayer structure are not linked to the avidin molecules of Giese's multilayer structure by covalent bonds. Since biotin is a ligand for avidin, it is expected that these two molecules are linked to one another by ionic interactions, hydrophobic interactions, hydrogen bonds, van der Waals forces or a combination of these non-covalent linkages.
4. Unlike the multimeric biopolymer of the present application, the multilayer structure of Giese does not comprise a plurality of proteins or polypeptides that have a binding region that is available for binding to a ligand or analyte. Because the Giese structure is formed by binding of the ligand, i.e. biotin, to the protein units of the Giese multilayer structure, all or nearly all of the ligand binding sites on the avidin molecules are occupied and are not available for binding to a ligand. Depending on whether the last layer in the Giese multilayer structure is a biotin molecule (or biotin-extender) or an avidin molecule, none or only one of the avidin molecules in Giese's multilayer structure has a binding region



## APPENDIX

1. (Currently Amended) A synthetic multimeric biopolymer comprising a plurality of monomeric units selected from the group consisting of proteins, polypeptides, nucleic acids, peptide nucleic acids, and combinations thereof;

wherein said monomeric units are covalently linked to each other;

wherein a plurality of said monomeric units of said multimeric biopolymer comprise a binding region which is available for binding to a ligand selected from the group consisting of a sugar, a peptide, a nucleic acid, a hormone, a vitamin, a co-factor, an anion other than a hydroxyl ion and a cation other than a hydrogen ion, and wherein each of said monomeric units exhibits a detectable conformational change in response to binding of the ligand to said binding region, the conformational change being detectable by NMR, X-ray crystallography or a biosensing system which detects a change in fluorescence of a reporter fluorophore that has been attached to said monomeric unit;

wherein said multimeric biopolymer exhibits a detectable change in its three-dimensional conformation when the ligand binds to one or more of the plurality of monomeric units that comprise a binding region for the ligand, and

wherein at least one of the monomeric units of said mulimeric biopolymer transmits a detectable signal selected from the group consisting of a fluorescent signal, an optical signal, an electrochemical signal, a pressure change, a dielectric constant change, a mass change, a volume change, and a temperature change in response to the change in the three-dimensional conformation of the biopolymer.

12. (Twice Amended) A synthetic multimeric biopolymer comprising two or more monomeric units selected from the group consisting of a protein, a polypeptide, a nucleic acid, and a peptide nucleic acid,

wherein said monomeric units are covalently linked to each other,

wherein the multimeric biopolymer comprises a plurality of monomeric units comprising a binding region which is available for binding to an analyte selected from the group consisting of a sugar, a peptide, a nucleic acid, a hormone, a vitamin, a co-factor, an anion other than a hydroxyl ion and a cation other than a hydrogen ion; and

wherein binding of the analyte to said binding region results in a change in conformation of said monomeric unit, said conformational change being detectable by NMR, X-ray crystallography or a biosensing system which detects a change in fluorescence of a reporter fluorophore that has been attached to said monomeric unit;

and wherein binding of the analyte to the binding region of said monomeric units results in the formation of protons or hydroxides or the transmission of a detectable signal by at least one other monomeric unit of the multimeric polymer.

41. (Once Amended) A synthetic multimeric biopolymer comprising two or more monomeric units selected from the group consisting of proteins, polypeptides, nucleic acids, peptide nucleic acids, and combinations thereof;

wherein said monomeric units are covalently linked to each other;

wherein a plurality of said monomeric units in said biopolymer comprise a binding region which is available for binding to an analyte selected from the group consisting of a sugar, a protein, a peptide, a nucleic acid, a hormone, a vitamin, a co-factor, an anion other than a hydroxyl ion and a cation other than a hydrogen ion;

wherein each of the monomeric units that comprise a binding region for an analyte exhibits a change its three-dimensional conformation in response to binding of the analyte to said monomeric unit, said conformational change being detectable by NMR, X-ray crystallography or a biosensing system which detects a change in fluorescence of a reporter fluorophore that has been attached to said monomeric unit ; and

wherein said multimeric biopolymer exhibits a greater change in its three-dimensional conformation in response to binding of the analyte to said binding region of said monomeric units than the conformational change that occurs in an individual monomeric unit as a result of binding of an analyte to said individual monomeric unit.